AMENDMENT TO THE CLAIMS

Claims 1-12. Cancel

13. (Original) A method of promoting recruitment, proliferation, differentiation, migration or survival of neural cells or neural precursor cells in a mammalian subject comprising:

identifying a mammalian subject in need of treatment to promote recruitment, proliferation, differentiation, migration, or survival of neural cells or neural precursor cells, and

administering to the subject a composition comprising a vascular endothelial growth factor C (VEGF-C) product or a vascular endothelial growth factor D (VEGF-D) product in an amount effective to stimulate recruitment, proliferation, differentiation, migration or survival of neural cells or neural precursor cells in said subject.

14. (Original) A method according to claim 13 wherein the identifying comprises identifying a mammalian subject in need of treatment to promote recruitment, proliferation, differentiation, migration or survival of neuronal cells or neuronal precursor cells.

15. (Original) A method according to claim 13, wherein the identifying comprises identifying a mammalian subject in need of oligodendrocyte or oligodendrocyte precursor cell recruitment, proliferation, or differentiation.

16. (Original) A method of promoting proliferation, differentiation, migration or survival of neural stem cells or neural precursor cells comprising:

contacting purified neural stem cells or neural precursor cells with a composition comprising a vascular endothelial growth factor C (VEGF-C) product or a vascular endothelial growth factor D (VEGF-D) product in an amount effective to promote survival or stimulate proliferation or differentiation of said cells.

17. (Original) A method according to claim 16, wherein the neural stem cell is selected from the group consisting of C17.2, purified neural stem cells, HSN-1 cells, fetal pig cells, neural crest cells, bone marrow derived neural stem cells, hNT cells and a human neuronal progenitor cell line.

18. (Original) A method of inducing oligodendrocyte precursor cell proliferation *in vitro* comprising contacting the oligodendrocyte or oligodendrocyte precursor cell with a composition comprising a VEGF-C product or a VEGF-D product, wherein the oligodendrocyte precursor cell is selected from the group consisting of CG-4 cells, SVG p12 fetal glial cell line, DBTRG-05MG glial cell line, purified oligodendrocyte precursor cells, isolated NG2 proteoglycan (NG2+ cells), bone marrow derived neural stem cells, a human neuronal progenitor cell line.

19. (Currently amended) A method of stimulating neural stem cell or neuronal precursor cell proliferation or differentiation, comprising,

obtaining a biological sample from a mammalian subject, wherein said sample comprises neural stem cells or neuronal precursor cells, and

contacting the neural stem cells or neuronal precursor cells with a composition comprising a vascular endothelial growth factor C (VEGF-C) product or a vascular endothelial growth factor D (VEGF-D) product.

20. (Cancel)

21. (Original) A method of stimulating oligodendrocyte precursor cell proliferation or differentiation, comprising,

obtaining a biological sample from a mammalian subject, wherein said sample comprises oligodendrocyte precursor cells, and

contacting the oligodendrocyte precursor cells with a composition comprising a vascular endothelial growth factor C (VEGF-C) product or a vascular endothelial growth factor D (VEGF-D) product.

22. (Currently amended) A method according to any one of claims 16-19 or 21 ~~16-21~~, wherein the contacting comprises culturing the cells in a culture containing the VEGF-C product or the VEGF-D product.

23. (Currently amended) A method according to claim 19 or 21 ~~any one of claims 19-22~~, further comprising a step of purifying and isolating the cells from the sample before the contacting step.

24. (Currently amended) A method according to claim 22 ~~any one of claims 16-23~~, further comprising a step of purifying and isolating the cells after the contacting step.

25. (Currently amended) Purified and isolated neural cells cultured according to claim 24 ~~any one of claims 16-24~~.

26. (Currently amended) The method according to claim 24 ~~any one of claims 19-24~~, further comprising a step of administering the cells to the mammalian subject after the contacting step.

27. (Currently amended) The method according to claim 24 ~~any one of claims 19-24~~ further comprising a step of transplanting the cells into a different mammalian subject after the contacting step.

28. (Cancel)

29. (Currently amended) The method according to claim 24 ~~of any one of claims 26-28~~, wherein the cells are seeded into a tissue, organ, or artificial matrix *ex vivo*, and said tissue, organ, or artificial matrix is attached, implanted, or transplanted into the mammalian subject.

30. (Currently amended) A method according to any one of claims 13-15 or ~~26~~-29, wherein the subject has a disease or condition characterized by aberrant growth of neuronal cells, neuronal scarring, or neural degeneration.

31. (Currently amended) A method according to claim 30, wherein the neural degeneration is caused by a neurodegenerative disorder selected from the group consisting of ~~is~~ Alzheimer's disease, Parkinson's disease, Huntington's disease, motor neuron disease, Amyotrophic Lateral Sclerosis (ALS), dementia and cerebral palsy.

32. (Currently amended) A method according to any one of claims 13-15 or ~~26~~-29, wherein the subject has a disease or condition characterized by aberrant growth of oligodendrocyte or oligodendrocyte precursor cells.

33. (Currently amended) A method according to any one of claims 13-15 or ~~26~~-29, wherein the subject has a condition selected from the group consisting of ~~characterized by~~ demyelination in the nervous system, chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), neural trauma or neural injury.

34. (Original) The method of claim 33 wherein the condition is multiple sclerosis, phenylketonuria, periventricular leukomalacia (PVL) HIV-1 encephalitis (HIVE), Guillian Barre Syndrome (GBS), acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN), Fisher syndrome, acute pandysautonomia, and Krabbe's disease.

35. (Cancel)

36. (Currently amended) The method of claim 33 ~~35~~ wherein the CIPD is selected from the group consisting of MADSAM (multifocal acquired demyelinating sensory and motor neuropathy, also know as Lewis-Sumner syndrome) and DADS (distal acquired demyelinating symmetric neuropathy).

37. (Cancel)

38. (Currently amended) The method of claim 33 ~~37~~, wherein the neural trauma is selected from the group consisting of stroke-related injury, spinal cord injury, post-operative injury and brain ischemia.

39. (Currently amended) The method of claim 13 ~~any one of claims 13-15 or 26-38~~, wherein the mammalian subject is human.

40. (Currently amended) The method ~~or use~~ according to claim 39 ~~any one of claims 1-24 or 26-28~~, wherein the product is a VEGF-C product.

41. (Currently amended) The method ~~or use~~ according to claim 40, wherein the VEGF-C product comprises a purified mammalian prepro-VEGF-C polypeptide or fragment thereof that binds VEGFR-3 or neuropilin-2.

42. (Currently amended) The method ~~or use~~ according to claim 40, wherein the VEGF-C product comprises a VEGF-C ΔC_{156} polypeptide.

43. (Currently amended) The method ~~or use~~ according to claim 40, wherein the VEGF-C product comprises a chimeric heparin-binding VEGF-C polypeptide.

44. (Original) The method of claim 40, wherein the subject and the prepro-VEGF-C polypeptide are human.

45. (Currently amended) The method ~~or use~~ according to claim 40, wherein the VEGF-C product comprises a polypeptide that comprises an amino acid sequence at least 95% identical to amino acids 32-227 of SEQ ID NO: 24, wherein the polypeptide binds VEGFR-3.

46. (Currently amended) The method ~~or use~~ according to claim 40, wherein the VEGF-C product comprises a polypeptide that comprises an amino acid sequence at least 95% identical to amino acids 103-227 of SEQ ID NO: 24, wherein the polypeptide binds VEGFR-3.

47. (Currently amended) The method ~~or use~~ of claim 40, wherein the VEGF-C product comprises a polynucleotide selected from:

(a) a polynucleotide comprising a nucleotide sequence at least 90% identical to the nucleotide sequence of SEQ ID NO: 23 and encoding a polypeptide that binds VEGFR-3;

(b) a polynucleotide comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence at least 90% identical to SEQ ID NO: 24, wherein the polypeptide binds VEGFR-3;

(c) a polynucleotide that hybridizes to the complement of SEQ ID NO: 23 under the following hybridization and washing conditions and encodes a polypeptide that binds VEGFR-3: hybridization in 0.5 M NaHPO4, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65° C and washing in 0.2 X SSC/0.1% SDS at 42° C

(d) a polynucleotide comprising a nucleotide sequence that encodes the human VEGF-C amino acid sequence of SEQ ID NO: 24;

(e) a polynucleotide that encodes a VEGF-C ΔC_{156}, polypeptide:

(f) a nucleotide sequence that encodes a chimeric heparin binding VEGF-C polypeptide; and

~~(b)~~ (g) fragments of (a), (b) or (d) that encode a polypeptide that binds VEGFR-3.

48-49. (Cancel)

50. (Original) The method or use of claim 40, wherein the VEGF-C product comprises a polynucleotide selected from:

(a) a polynucleotide comprising a nucleotide sequence that encodes the human VEGF-C amino acid sequence of SEQ ID NO: 24; and

(b) fragments of (a) that encode a polypeptide that binds VEGFR-3.

51-52. (Cancel)

53. (Currently amended) The method ~~or use~~ according to claim 47 ~~any one of claims 47-52~~, wherein the VEGF-C product comprises a viral vector containing the polynucleotide.

54. (Currently amended) The method ~~or use~~ of claim 53, wherein the vector comprises a replication-deficient adenovirus, adeno-associated virus, or lentivirus.

55. (Currently amended) The method ~~or use~~ according to claim 39 ~~any one of claims 1-24 or 26-39~~, wherein the product is a VEGF-D product.

56. (Currently amended) A method ~~or use~~ according to any one of claims 40 or 55 ~~1-24 or 26-55~~, wherein the composition further comprises a pharmaceutically acceptable carrier.

57. (Currently amended) The method of any one of claims ~~13-24 or 26-55~~ 40 or 55, further comprising administering to the mammalian subject a neurotherapeutic agent.

58. (Cancel)

59. (Currently amended) The method ~~or use~~ according to claim 57 ~~any one of claims 57-58~~ wherein the neurotherapeutic agent comprises a neural growth factor selected from the group consisting of interferon gamma, nerve growth factor, epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), neurogenin, brain derived neurotrophic factor (BDNF), thyroid hormone, bone morphogenic proteins (BMPs), leukemia inhibitory factor (LIF), sonic hedgehog, glial cell line-derived neurotrophic factor (GDNFs), vascular endothelial growth factor (VEGF), interleukins, interferons, stem cell factor (SCF), activins, inhibins, chemokines, retinoic acid and ciliary neurotrophic factor (CNTF).

60. (Currently amended) The method ~~or use~~ according to claim 57 ~~any one of claims 57-58~~, wherein the neurotherapeutic agent comprises a polynucleotide comprising a nucleotide sequence that encodes a neural growth factor selected from the group consisting of interferon gamma, nerve growth factor, epidermal growth factor (EGF), basic fibroblast growth factor (bFGF), neurogenin, brain derived neurotrophic factor (BDNF), thyroid hormone, bone morphogenic proteins (BMPs), leukemia inhibitory factor (LIF), sonic hedgehog, glial cell line-derived neurotrophic factor (GDNFs), vascular endothelial growth factor (VEGF), interleukins, interferons, stem cell factor (SCF), activins, inhibins, chemokines, retinoic acid and ciliary neurotrophic factor (CNTF).

61. (Currently amended) The method ~~or use~~ according to claim 57 ~~or 58~~, wherein the neurotherapeutic agent is selected form the group consisting of tacrine ~~(Cognex)~~, donepezil ~~(Aricept)~~, rivastigmine ~~(Exelon)~~, galantamine ~~(Reminyl)~~, cholinesterase inhibitors and anti-inflammatory drugs.

62. (Currently amended) The method ~~or use~~ of claim 57 ~~or 5758~~ wherein the neurotherapeutic agent is selected form the group consisting of anti-cholinergics, dopamine agonists, catechol-0-methyl-transterases (COMTs), amantadine ~~(Symmetrel)~~, ~~Sinemet®~~, Selegiline, carbidopa, ropinirole, ~~(Requip).~~ coenzyme Q10, Pramipexole ~~(Mirapex)~~ and levodopa (L-dopa).

63. (Currently amended) The method ~~or use~~ of any one of claims 40 or 55 ~~1-24 or 26-62~~ wherein the VEGF-C or VEGF-D product is used or administered in combination with PDGF-A or PDGF-C.

64. (Currently amended) A composition comprising a VEGF-C product or a VEGF-D product and a neural growth factor in a pharmaceutically acceptable diluent or carrier.

65. (Currently amended) A composition comprising a VEGF-C product or a VEGF-D product and a neurotherapeutic agent in a pharmaceutically acceptable diluent or carrier.

66-67. (Cancel)

68. (Currently amended) A composition of claim 64 or 65 ~~any one of claims 64-67~~, further comprising a PDGF-A product or a PDGF-C product.

69. (cancel)

70. (Original) A method of inhibiting growth and progression and of neuroblastoma and neural tumors comprising administering to a subject having a neuroblastoma or neuronal tumor a composition comprising a VEGF-C inhibitor.

71. (Currently amended) The method ~~or use~~ of claim ~~69 or~~ 70 wherein the VEGF-C inhibitor is selected from the group consisting of:

(a) a polypeptide comprising an extracellular fragment of VEGFR-2 that binds to VEGF-C;

(b) a polypeptide comprising an extracellular fragment of VEGFR-3 that binds to VEGF-C;

(c) an antibody substance that immunoreacts with a VEGF-C polypeptide;

(d) a VEGF-C antisense molecule, and

(e) a VEGF-C siRNA.

72. (Currently amended) The method ~~or use~~ of claim ~~69 or~~ 70, wherein the VEGF-C inhibitor is selected from the group consisting of a polypeptide comprising an extracellular fragment of VEGFR-3 that binds to VEGF-C, an extracellular fragment of NRP-1 that binds to VEGF-C, and an extracellular fragment of NRP-2 that binds to VEGF-C.

73. (Currently amended) The method ~~or use~~ of any one of claims 70-72 ~~67-70~~ wherein the VEGF-C or VEGF-D ~~product~~ inhibitor is ~~used or~~ administered in combination with a PDGF-A inhibitor or a PDGF-C inhibitor.

74. (Currently amended) A method for screening for modulators of VEGF-C or VEGF-D stimulation of neural stem cell or neural precursor cell growth, migration, differentiation, or survival, comprising:

contacting a composition comprising a VEGF-C polypeptide or a VEGF-D polypeptide and a neural cell or neural precursor cell in the presence and absence of a test agent;

measuring growth, migration, differentiation, or survival of the cell in the presence and absence of the agent; and

identifying the test agent as a modulator of VEGF-C or VEGF-D effects on neural cells or neural precursor cells from differential measurements in the presence versus the absence of the test agent.

75. (Cancel)

76. (Currently amended) The method of claim 74 ~~or 75~~ wherein the cell comprises a neural stem cell line.

77. (Currently amended) The method of claim 74 ~~or 75~~ wherein the cell comprises neural cell or neural progenitor cell that expresses VEGFR-3.

78. (Currently amended) The method of claim 74 ~~any one of claim 74, 75 or 76~~ wherein the cell expresses neuropilin 2.

79. (Currently amended) The method of claim 74 ~~or 75~~ for detecting a modulator that is an agonist of stimulation of neural stem cell or neural precursor cell growth, migration, differentiation, or survival,

wherein an agonist is detected by an increase in staining of neural cell markers on the cell surface or increased detection of proliferative markers in the cell.

~~70~~ 80. (Currently amended) The method of claim 74 ~~or 75~~ for detecting a modulator that is an antagonist of stimulation of neural stem cell or neural precursor cell growth, migration, differentiation, or survival,

wherein an antagonist is detected by a decrease in staining of neural cell markers on the cell surface or decreased detection of proliferative markers in the cell.

81. (New) A method according to claim 23, further comprising a step of purifying and isolating the cells after the contacting step.